09/973,981

[redacted]

* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 16:25:44 ON 21 MAY 2003

=> file biosis medline caplus wpids uspatfull

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'BIOSIS' ENTERED AT 16:26:06 ON 21 MAY 2003
COPYRIGHT (C) 2003 BIOLOGICAL ABSTRACTS INC.(R)

FILE 'MEDLINE' ENTERED AT 16:26:06 ON 21 MAY 2003

FILE 'CAPLUS' ENTERED AT 16:26:06 ON 21 MAY 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'WPIDS' ENTERED AT 16:26:06 ON 21 MAY 2003
COPYRIGHT (C) 2003 THOMSON DERWENT

FILE 'USPATFULL' ENTERED AT 16:26:06 ON 21 MAY 2003
CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

*** YOU HAVE NEW MAIL ***

=> s oligo? (3a) (folic or folate) conjugate?
MISSING OPERATOR FOLATE) CONJUGATE?
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s oligo? (3a) (folic or folate) (4a) conjugate?
L1 29 OLIGO? (3A) (FOLIC OR FOLATE) (4A) CONJUGATE?

=> d l1 bib abs 1-29

L1 ANSWER 1 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2003:172941 BIOSIS
DN PREV200300172941
TI **Oligonucleotide-folate conjugates.**
AU Cook, Phillip Dan; Manoharan, Muthiah; Bhat, Balkrishen
ASSIGNEE: Isis Pharmaceuticals, Inc.
PI US 6528631 March 04, 2003
SO Official Gazette of the United States Patent and Trademark Office Patents, (Mar. 4 2003) Vol. 1268, No. 1, pp. No Pagination.
http://www.uspto.gov/web/menu/patdata.html. e-file.
ISSN: 0098-1133.
DT Patent
LA English
AB **Oligonucleotide-folate conjugates** are described wherein folates are conjugated to one or more sites on an oligonucleotide including the 2'-, 3'-, 5'-, nucleobase and internucleotide linkage sites. The folate can be attached via the alpha- or gamma-carboxylate, optionally through a linking group. Methods for the regiospecific synthesis of the conjugates are disclosed.

L1 ANSWER 2 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2002:144705 BIOSIS
DN PREV200200144705
TI Nucleosidic and non-nucleosidic folate conjugates.
AU Guzaev, Andrei P. (1); Cook, Phillip Dan; Manoharan, Muthiah; Bhat,

09567863

Balkrishen
CS (1) Carlsbad, CA USA
ASSIGNEE: ISIS Pharmaceuticals, Inc.,, Carlsbad, CA, USA
PI US 6335434 January 01, 2002
SO Official Gazette of the United States Patent and Trademark Office Patents, (Jan. 1, 2002) Vol. 1254, No. 1, pp. No Pagination. http://www.uspto.gov/web/menu/patdata.html. e-file. ISSN: 0098-1133.
DT Patent
LA English
AB **Oligonucleotide-folate conjugates** are described wherein folates are conjugated to one or more sites on an oligonucleotide including the 2'-, 3'-, 5'-, nucleobase and internucleotide linkage sites. The folate can be attached via the alpha- or gamma-carboxylate, optionally through a linking group. Methods for the regiospecific synthesis of the conjugates are diclosed. Also disclosed are nucleosidic and non-nucleosidic linkers conjugated to folic acid and related folates.

L1 ANSWER 3 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1994:213766 BIOSIS
DN PREV199497226766
TI Inhibition of leukaemia cell proliferation by folic acid-polylysine-mediated introduction of c-myb antisense oligodeoxynucleotides into HL-60 cells.
AU Citro, G. (1); Szczylik, C.; Ginobbi, P.; Zupi, G.; Calabretta, B.
CS (1) Lab. Chimioterapia Sperimentale, Ist. Tumori Regina Elena Roma, Via delle Messi D'Oro 156, 00158 Rome Italy
SO British Journal of Cancer, (1994) Vol. 69, No. 3, pp. 463-467. ISSN: 0007-0920.
DT Article
LA English
AB The inhibitory effect of c-myb antisense **oligodeoxynucleotides** (ODNs) **conjugated** to **folic** acid (FA) on HL-60 cell proliferation was examined. Folic acid was covalently linked to a polylysine chain and purified by gel chromatography. Sterile FA-polylysine was complexed with c-myb sense and antisense. Exposure of HL-60 cells to the FA-polylysine-c-myb antisense ODN complex resulted in a down-regulation of c-myb expression and a greater inhibition of proliferation than that obtained using free ODNs. Moreover, FA-polylysine conjugate alone or complexed to c-myb sense ODN was not toxic to cells. The antigenic properties and uptake of the vitamin were not affected by the polylysine chain. These data suggest that this strategy is potentially useful for the selective delivery of anti-oncogene-targeted ODNs into cancer cells.

L1 ANSWER 4 OF 29 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1972:216983 BIOSIS
DN BA54:46977
TI THE SYNTHESIS OF BIOLOGICALLY ACTIVE PTEROYL **OLIGO**-GAMMA-L GLUTAMATES **FOLIC**-ACID **CONJUGATES** EVALUATION OF TRITIATED PTEROYL HEPTA GLUTAMATE FOR METABOLIC STUDIES.
AU GODWIN H A; ROSENBERG I H; FERENZ C R; JACOBS P M; MEIENHOFER J
SO J BIOL CHEM, (1972) 247 (8), 2266-2271. CODEN: JBCHA3. ISSN: 0021-9258.
FS BA; OLD
LA Unavailable

L1 ANSWER 5 OF 29 MEDLINE
AN 94168950 MEDLINE
DN 94168950 PubMed ID: 8123474
TI Inhibition of leukaemia cell proliferation by folic acid-polylysine-

09567863

mediated introduction of c-myb antisense oligodeoxynucleotides into HL-60 cells.

AU Citro G; Szczylik C; Ginobbi P; Zupi G; Calabretta B

CS Laboratorio Chemioterapia Sperimentale, Istituto Tumori Regina Elena, Roma, Italy.

SO BRITISH JOURNAL OF CANCER, (1994 Mar) 69 (3) 463-7.
Journal code: 0370635. ISSN: 0007-0920.

CY SCOTLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199404

ED Entered STN: 19940420
Last Updated on STN: 20000303
Entered Medline: 19940414

AB The inhibitory effect of c-myb antisense **oligodeoxynucleotides** (ODNs) **conjugated** to **folic** acid (FA) on HL-60 cell proliferation was examined. Folic acid was covalently linked to a polylysine chain and purified by gel chromatography. Sterile FA-polylysine was complexed with c-myb sense and antisense. Exposure of HL-60 cells to the FA-polylysine-c-myb antisense ODN complex resulted in a down-regulation of c-myb expression and a greater inhibition of proliferation than that obtained using free ODNs. Moreover, FA-polylysine conjugate alone or complexed to c-myb sense ODN was not toxic to cells. The antigenic properties and uptake of the vitamin were not affected by the polylysine chain. These data suggest that this strategy is potentially useful for the selective delivery of anti-oncogene-targeted ODNs into cancer cells.

L1 ANSWER 6 OF 29 CAPLUS COPYRIGHT 2003 ACS

AN 2003:168856 CAPLUS

DN 138:170466

TI Regioselective solid phase preparation of **oligonucleotide-folate conjugates**

IN Cook, Phillip Dan; Manoharan, Muthiah; Bhat, Balkrishen

PA Isis Pharmaceuticals, Inc., USA

SO U.S., 59 pp., Cont.-in-part of U.S. Ser. No. 117,363.
CODEN: USXXAM

DT Patent

LA English

FAN.CNT 104

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6528631	B1	20030304	US 1998-98166	19980616
	CA 2170869	AA	19950309	CA 1994-2170869	19940902
	AU 713740	B2	19991209	AU 1997-26244	19970624
	AU 9726244	A1	19971106		
	US 6232463	B1	20010515	US 1998-128508	19980804
	US 6335434	B1	20020101	US 1999-275505	19990324
	WO 9966063	A2	19991223	WO 1999-US13565	19990616
	WO 9966063	A3	20000420		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1993-117363 A2 19930903
AU 1993-38025 A3 19930225

09567863

US 1997-948151 A1 19971009
US 1998-98166 A2 19980616
US 1999-275505 A 19990324

OS MARPAT 138:170466

AB **Oligonucleotide-folate conjugates** are described wherein folates are conjugated to one or more sites on an oligonucleotide including the 2'-, 3'-, 5'-, nucleobase and internucleotide linkage sites. The folate can be attached via the .alpha.- or .gamma.-carboxylate, optionally through a linking group. Methods for the regiospecific synthesis of the conjugates are disclosed. Thus, 5'-O-DMT-2'-O-aminohexyl-5-methyl-uridine-N2-ibu-N10-trifluoroacetyl-.alpha.-allyl-folic acid-.gamma.-conjugate 3'-phosphoramidite was prepd. and incorporated into oligodeoxyribonucleotides.

RE.CNT 246 THERE ARE 246 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 7 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 2002:516827 CAPLUS
DN 137:185756
TI Synthesis of N-Acetyl-D-galactosamine and Folic Acid Conjugated Ribozymes
AU Matulic-Adamic, Jasenka; Serebryany, Vladimir; Haeberli, Peter; Mokler, Victor R.; Beigelman, Leonid
CS Department of Chemistry Biochemistry, Ribozyme Pharmaceuticals Inc., Boulder, CO, 80301, USA
SO Bioconjugate Chemistry (2002), 13(5), 1071-1078
CODEN: BCCHES; ISSN: 1043-1802
PB American Chemical Society
DT Journal
LA English
OS CASREACT 137:185756
AB To evaluate potential improvement in tissue specific targeting and cellular uptake of therapeutic ribozymes, we have developed three new phosphoramidite reagents. These reagents can be used in automated solid-phase synthesis to produce oligonucleotide conjugates contg. N-acetyl-D-galactosamine (targeting hepatocytes) and folic acid (targeting tumor). N-Acetyl-D-galactosamine was attached through a linker to both 2'-amino-2'-deoxyuridine and D-threoninol scaffolds, and these conjugates were converted to phosphoramidite building blocks. Incorporation of a D-threoninol-based monomer into ribozymes provided multiply labeled ribozyme conjugates. Attachment of the fully protected pteroic acid to the D-threoninol-6-aminocaproyl-L-glutamic acid construct afforded the folic acid conjugate, which was converted into the phosphoramidite and incorporated onto the 5'-end of the ribozyme.

RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 8 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 2002:6385 CAPLUS
DN 136:86030
TI Preparation of nucleosidic and non-nucleosidic **oligodeoxyribonucleotide-folate conjugates**
IN Guzaev, Andrei P.; Cook, Phillip Dan; Manoharan, Muthiah; Bhat, Balkrishen
PA Isis Pharmaceuticals, Inc., USA
SO U.S., 88 pp., Cont.-in-part of U. S. Ser. No. 98,166.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 104

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6335434	B1	20020101	US 1999-275505	19990324
	AU 713740	B2	19991209	AU 1997-26244	19970624

09567863

AU 9726244	A1	19971106			
US 6528631	B1	20030304	US 1998-98166	19980616	
US 6232463	B1	20010515	US 1998-128508	19980804	
WO 9966063	A2	19991223	WO 1999-US13565	19990616	
WO 9966063	A3	20000420			

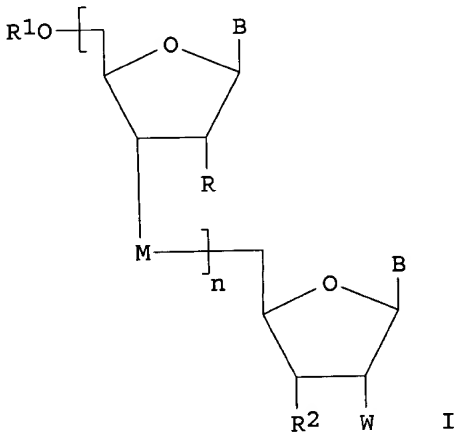
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002049163	A1	20020425	US 2001-973981	20011009	
PRAI US 1998-98166	A2	19980616			
AU 1993-38025	A3	19930225			
US 1993-117363	A2	19930903			
US 1997-948151	A1	19971009			
US 1999-275505	A	19990324			

OS MARPAT 136:86030

GI



I

AB **Oligonucleotide-folate conjugates** I wherein B is a nucleobase; R is aminooxoyalkoxy; R1 is H, hydroxyl protecting group; R2 is H, phosphoramidite; M is optionally protected internucleoside linkage; W is non-nucleosidic linker substituted heteroaryl; are described wherein folates are conjugated to one or more sites on an oligonucleotide including the 2'-, 3'-, 5'-nucleobase and internucleotide linkage sites. The folate can be attached via the .alpha.- or .gamma.-carboxylate, optionally through a linking group. Also disclosed are nucleosidic and non-nucleosidic linkers conjugated to folic acid and related folates. Thus, 5'-O-DMT-2'-O-aminohexyl-5-methyl-uridine-N2-ibu-N10-trifluoroacetyl-a-allyl-folic acid-g-conjugate 3'-phosphoramidite was prepd. and incorporated into oligodeoxyribonucleotides.

RE.CNT 250 THERE ARE 250 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 9 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 1999:811380 CAPLUS
DN 132:50215
TI Preparation of nucleosidic and non-nucleosidic

09567863

oligodeoxyribonucleotide-folate conjugates

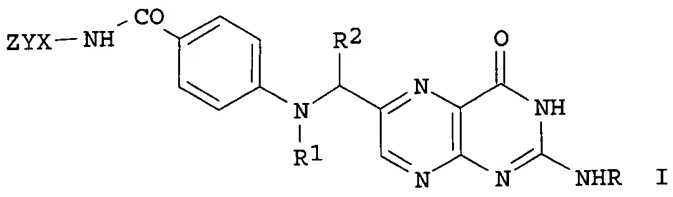
IN Manoharan, Muthiah; Bhat, Balkrishen; Cook, Phillip Dan; Guzaev, Andrei P.
PA Isis Pharmaceuticals, Inc., USA

SO PCT Int. Appl., 207 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 104

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9966063	A2	19991223	WO 1999-US13565	19990616
	WO 9966063	A3	20000420		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 713740	B2	19991209	AU 1997-26244	19970624
	AU 9726244	A1	19971106		
	US 6528631	B1	20030304	US 1998-98166	19980616
	US 6232463	B1	20010515	US 1998-128508	19980804
	US 6335434	B1	20020101	US 1999-275505	19990324
PRAI	US 1998-98166	A	19980616		
	US 1999-275505	A	19990324		
	AU 1993-38025	A3	19930225		
	US 1993-117363	A2	19930903		
	US 1997-948151	A1	19971009		

OS MARPAT 132:50215

GI



I

AB **Oligonucleotide-folate conjugates** I wherein:
X is the side chain of a naturally-occurring or non- naturally-occurring amino acid, or a protected side chain of a naturally-occurring or non-naturally-occurring amino acid, substituted alkyl; Y is N(Z1)C(O), C(O)NH, NHC(O), OC(O)NH, C(S)NH, SC(S)NH, SC(O)NH, OC(S)NH, C(O)O, C(O)(CH2)n or a bond; n is an integer from 1 to 50; each Z and Z1 is, independently, hydrogen or a hydrocarbyl group selected from alkyl, alkenyl, alkynyl, aryl, aralkyl, cycloalkyl, fused cycloalkyl, heterocycle, heterocyclylalkyl, heteroaryl and heteroarylalkyl; wherein said hydrocarbyl group is substituted with at least two hydroxyl groups, and is optionally substituted with oxo, acyl, alkoxy, alkoxycarbonyl, alkyl, alkenyl, alkynyl, amino, amido, azido, aryl, heteroaryl, carboxylic acid, cyano, guanidino, halo, haloalkyl, haloalkoxy, hydrazino, ODMT, alkylsulfonyl, nitro, sulfide, disulfide, sulfone, sulfonate, sulfonamide, thiol, and thioalkoxy; R is H, amino protecting group; R1 is hydrogen, alkyl, alkenyl, alkynyl, aryl or an amino-protecting group; R2 is hydrogen, alkyl, alkenyl, alkynyl, aryl, aralkyl, cycloalkyl,

formyl,aminoalkyl, hydroxymethylare described wherein folates are conjugated to one or more sites on an oligonucleotide including the 2'-, 3'-, 5'-, nucleobase and internucleotide linkage sites. The folate can be attached via the .alpha.- or .gamma.-carboxylate, optionally through a linking group. Methods for the regiospecific synthesis of the conjugates are disclosed. Also disclosed are nucleosidic and non-nucleosidic linkers conjugated to folic acid and related folates. Thus, [N6-Benzoyl-5'-O-(4,4'-dimethoxytrityl)-adenylyl]-2'-O-(pentylamino)-N2-isobutyryl-N1-trifluoroacetyl-a-O-methyl-folic acid was prepd. and incorporated into oligodeoxyribonucleotides.

L1 ANSWER 10 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 1999:514957 CAPLUS
DN 131:257809
TI Synthesis of fully protected nucleoside-folic acid conjugated phosphoramidites and their incorporation into antisense oligonucleotides
AU Bhat, Balkrishen; Balow, Guity; Guzaev, Andrei; Cook, P. Dan; Manoharan, Muthiah
CS Department of Medicinal Chemistry, Isis Pharmaceuticals, Carlsbad, CA, 92008, USA
SO Nucleosides & Nucleotides (1999), 18(6 & 7), 1471-1472
CODEN: NUNUD5; ISSN: 0732-8311
PB Marcel Dekker, Inc.
DT Journal
LA English
AB A symposium on synthesis of the nucleoside-folic acid conjugates. This approach allowed us to synthesize several analogs, which were converted to phosphoramidites and successfully incorporated into therapeutically active antisense oligonucleotides.
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 11 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 1998:665280 CAPLUS
DN 130:43219
TI Folate-mediated targeting of antisense oligodeoxynucleotides to ovarian cancer cells
AU Li, Song; Deshmukh, Hemant M.; Huang, Leaf
CS Laboratory of Drug Targeting, Department of Pharmacology, University of Pittsburgh School of Medicine, Pittsburgh, PA, 15261, USA
SO Pharmaceutical Research (1998), 15(10), 1540-1545
CODEN: PHREEB; ISSN: 0724-8741
PB Plenum Publishing Corp.
DT Journal
LA English
AB Receptors for vitamin folic acid are frequently overexpressed on epithelial cancer cells, esp. ovarian cancer cells. In this study, we examd. whether this expression might be exploited to specifically deliver antisense oligodeoxynucleotides (ODN) to tumor cells. A conjugate was prepd. by directly coupling folic acid to the 3' terminus of an anti-c-fos ODN and its cellular uptake and tumor inhibitory effect were evaluated using FD2008 cells that overexpress folate receptors. When a phosphorothioate (PS)/phosphodiester (PO) chimeric ODN was conjugated with folic acid, its uptake by FD2008 cells was increased by about 8-fold ($P < 0.01$). In contrast, conjugation of folate to the ODN did not increase its uptake by CHO cells that lack the expression of FBP ($P > 0.05$). Furthermore, the increase in the uptake of conjugated ODN by FD2008 cells could be blocked by adding an excess amt. of folic acid. The PS/PO antisense ODN had some inhibitory effect on the growth of FD2008 cells. However, its activity was significantly increased following conjugation with folic acid ($P < 0.01$). ODN of scrambled sequences with and without conjugation with folic acid failed to inhibit the growth of FD2008 cells.

Finally, the antisense effect of the conjugated ODN on FD2008 cells was inhibited by an excess amt. of free folic acid, suggesting that the sequence-dependent effect of folate-antisense ODN conjugate was mediated by folate binding protein. Direct derivatization of ODN with folate significantly improves their targeting efficiency to tumor cells in vitro. The folate-conjugated ODN, due to their small size and possibly efficient extravasation at tumor site, has the potential for treating solid tumors that overexpress folate receptors.

RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 12 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 1995:510475 CAPLUS
DN 123:421
TI Delivery of antisense oligodeoxyribonucleotides against the human epidermal growth factor receptor into cultured KB cells with liposomes conjugated to folate via polyethylene glycol
AU Wang, Susan; Lee, Robert J.; Cauchon, Greg; Gorenstein, David G.; Low, Philip S.
CS Dep. of Chemistry, Purdue Univ., West Lafayette, IN, 47907, USA
SO Proceedings of the National Academy of Sciences of the United States of America (1995), 92(8), 3318-22
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
AB Antisense oligodeoxyribonucleotides targeted to the epidermal growth factor (EGF) receptor were encapsulated into liposomes linked to folate via a polyethylene glycol spacer (folate-PEG-liposomes) and efficiently delivered into cultured KB cells via folate receptor-mediated endocytosis. The oligonucleotides were a phosphodiester 15-mer antisense to the EGF receptor (EGFR) gene stop codon (AEGFR2), the same sequence with three phosphorothioate linkages at each terminus (AEGFR2S), a randomized 15-mer control of similar base compn. to AEGFR2 (RC15), a 14-mer control derived from a symmetrized Escherichia coli lac operator (LACM), and the 5'-fluorescein-labeled homologs of several of the above. Cellular uptake of AEGFR2 encapsulated in folate-PEG-liposomes was nine times higher than AEGFR2 encapsulated in nontargeted liposomes and 16 times higher than unencapsulated AEGFR2. Treatment of KB cells with AEGFR2 in folate-PEG-liposomes resulted in growth inhibition and significant morphol. changes. Curiously, AEGFR2 and AEGFR2S encapsulated in folate-PEG-liposomes exhibited virtually identical growth inhibitory effects, reducing KB cell proliferation by >90% 48 h after the cells were treated for 4 h with 3 .mu.M oligonucleotide. Free AEGFR2 caused almost no growth inhibition, whereas free AEGFR2S was only one-fifth as potent as the folate-PEG-liposome-encapsulated oligonucleotide. Growth inhibition of the oligonucleotide-treated cells was probably due to reduced EGFR expression because indirect immunofluorescence staining of the cells with a monoclonal antibody against the EGFR showed an almost quant. redn. of the EGFR in cells treated with folate-PEG-liposome-entrapped AEGFR2. These results suggest that antisense oligonucleotide encapsulation in folate-PEG-liposomes promise efficient and tumor-specific delivery and that phosphorothioate oligonucleotides appear to offer no major advantage over native phosphodiester DNA when delivered by this route.

L1 ANSWER 13 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 1994:595099 CAPLUS
DN 121:195099
TI Inhibition of leukemia cell proliferation by folic acid-polylysine-mediated introduction of c-myb antisense oligodeoxynucleotides into HL-60 cells
AU Citro, G.; Szczylik, C.; Ginobbi, P.; Zupi, G.; Calabretta, B.

09567863

CS Lab. Chemioterapia Sper., Ist. Tumori Regina Elena, Rome, 00158, Italy
SO British Journal of Cancer (1994), 69(3), 463-7
CODEN: BJCAAI; ISSN: 0007-0920
DT Journal
LA English
AB The inhibitory effect of c-myb antisense **oligodeoxynucleotides** (ODNs) **conjugated** to **folic** acid (FA) on HL-60 cell proliferation was examd. Folic acid was covalently linked to a polylysine chain and purified by gel chromatog. Sterile FA-polylysine was complexed with c-myb sense and antisense. Exposure of HL-60 cells to the FA-polylysine-c-myb antisense ODN complex resulted in a down-regulation of c-myb expression and a greater inhibition of proliferation than that obtained using free ODNs. Moreover, Fa-polylysine conjugate alone or complexes to c-myb sense ODN was not toxic to cells. The antigenic properties and uptake of the vitamin were not affected by the polylysine chain. These data suggest that this strategy is potentially useful for the selective delivery of anti-oncogene-targeted ODNs into cancer cells.

L1 ANSWER 14 OF 29 CAPLUS COPYRIGHT 2003 ACS
AN 1994:236162 CAPLUS
DN 120:236162
TI Dual action 2',5'-oligoadenylate antiviral derivatives and uses thereof
IN Suhadolnik, Robert J.; Pfleiderer, Wolfgang
PA Temple University, USA
SO PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9317692	A1	19930916	WO 1993-US1446	19930218
	W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
	AU 9337237	A1	19931005	AU 1993-37237	19930218
	AU 664883	B2	19951207		
	EP 630249	A1	19941228	EP 1993-906054	19930218
	EP 630249	B1	20020918		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 07504900	T2	19950601	JP 1993-515698	19930218
	AT 224196	E	20021015	AT 1993-906054	19930218
	IL 104886	A1	19970610	IL 1993-104886	19930228
	CN 1038592	B	19980603	CN 1993-101986	19930311
	CN 1191753	A	19980902	CN 1997-122682	19971114
PRAI	US 1992-849865	A	19920312		
	WO 1993-US1446	A	19930218		

OS MARPAT 120:236162
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Viral infection is inhibited in mammals by administration of metabolically stable, nontoxic 2',5'-oligoadenylate (2-5A) derivs. I (R = H; X = C1-6 alkyl or alkoxy; n = 1-8; m = 0-3) or pharmaceutically acceptable salts that have a dual therapeutic effect. The compds. activate the 2-5A synthetase/RNase L antiviral pathway of the mammal and also inhibit viral DNA polymerase. Conjugates of 2-5A derivs. with an adduct resulting in

enhanced penetration into intact cells (e.g. with a vitamin having a corresponding cell surface receptor for receptor-mediated endocytosis of the vitamin) for therapeutic delivery are also described.
2',5'-Cordycepin analogs contg. 3'-terminal acyclic nucleoside were prepd. as NH4 salts. The 2',5'-cordycepin trimer core and 5'-monophosphate (1 .mu.M), when incorporated into antibody-targeted liposomes specific for the T-cell receptor mol. CD3, inhibited 90% of HIV-1 replication.

L1 ANSWER 15 OF 29 WPIDS (C) 2003 THOMSON DERWENT
AN 2000-160501 [14] WPIDS
DNC C2000-050058
TI Novel conjugates with improved therapeutic properties including improved transfer across cellular membranes.
DC A25 A26 A96 B02 B04 D16
IN BHAT, B; COOK, P D; GUZZEV, A P; MANOHARAN, M; GUZAEV, A P
PA (ISIS-N) ISIS PHARM INC
CYC 86
PI WO 9966063 A2 19991223 (200014)* EN 207p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9945706 A 20000105 (200024)
US 6335434 B1 20020101 (200207)
US 2002049163 A1 20020425 (200233)
US 6528631 B1 20030304 (200320)
ADT WO 9966063 A2 WO 1999-US13565 19990616; AU 9945706 A AU 1999-45706 19990616; US 6335434 B1 CIP of US 1998-98166 19980616, US 1999-275505 19990324; US 2002049163 A1 Div ex US 1999-275505 19990324, US 2001-973981 20011009; US 6528631 B1 CIP of US 1993-117363 19930903, US 1998-98166 19980616
FDT AU 9945706 A Based on WO 9966063
PRAI US 1999-275505 19990324; US 1998-98166 19980616; US 2001-973981 20011009; US 1993-117363 19930903
AN 2000-160501 [14] WPIDS
AB WO 9966063 A UPAB: 20000320
NOVELTY - New nucleosidic and non-nucleosidic folate conjugates.
DETAILED DESCRIPTION - Nucleosidic and non-nucleosidic folate conjugates are of formula (I).
X4 = group of formula (i) or optionally protected side-chain of (non)naturally occurring amino acid;
X5 = N(X6')C(O), C(O)NH, NHC(O), OC(O)NH, C(S)NH, SC(S)NH, SC(O)NH, OC(S)NH, C(O)O, C(O)(CH2)n or bond;
n = 1-50;
X6, X6' = H or 1-10C alkyl, 2-10C alkenyl, 6-14C aryl, 6-14C aralkyl, 3-14C cycloalkyl, 5-14C fused cycloalkyl, 4-14C heterocyclyl, 4-14C heterocyclylalkyl, 4-14C heteroaryl or 4-14C heteroarylalkyl (all optionally substituted by oxo, acyl, alkoxy, alkoxycarbonyl, alkyl, alkenyl, alkynyl, amino, amido, azido, aryl, heteroaryl, carboxylic acid, cyano, guanidine, halo, haloalkyl, haloalkoxy, hydrazino, ODMT, alkylsulfonyl, nitro, sulfide, disulfide, sulfone, sulfonate, sulfonamide, thiol or thioalkoxy, provided that X6 is not H);
R4 = optionally protected hydroxy;
R5' = H, 1-10C alkyl, 2-10C alkenyl, 2-20C alkynyl, 6-14C aryl or amino-protecting group;
R5'' = H, 1-10C alkyl, 2-10C alkenyl, 2-20C alkynyl, 6-14C aryl, 6-14C aralkyl, 3-14C cycloalkyl, formyl, aminoalkyl or hydroxymethyl;
R6 = H or amino-protecting group; and
t = 1-2.
INDEPENDENT CLAIMS are also included for the following:

(1) preparation of folic acid derivative by reacting folic acid with reagent effective to form pterin aldehyde;

(2) folate conjugates comprising folate group covalent linked to amino acid that is further connected to hydrocarbyl group comprising at least two hydroxyl groups; and

(3) **oligonucleotide folate conjugate** comprising **folate** group linked to amino acid that is further connected to hydrocarbyl group comprising at least two hydroxyl groups.

USE - The nucleosidic and non-nucleosidic folate conjuagtes are used in antisense therapeutics in unicellular prokaryotic and eukaryotic organisms that utilize DNA-RNA transcription of RNA-protein translation as fundamental part of hereditary, metabolic or cellular control including bacteria, yeast, protozoa, algae and all plant and higher animal forms including warm blooded animals. They can also be used as research reagents, e.g. to elucidate function of genes, diagnostic aids and therapeutic agents.

ADVANTAGE - Improved therapeutic properties including improved transfer across cellular membranes.

Dwg.0/0

L1 ANSWER 16 OF 29 USPATFULL
AN 2003:120802 USPATFULL
TI Bioadhesive compositions and methods for enhanced intestinal drug absorption
IN Teng, Ching-Leou, San Diego, CA, UNITED STATES
Weinbch, Susan, San Diego, CA, UNITED STATES
Tillman, Lloyd G., Carlsbad, CA, UNITED STATES
Geary, Richard S., Carlsbad, CA, UNITED STATES
Hardee, Gregory E., Rancho Santa Fe, CA, UNITED STATES
PI US 2003083286 A1 20030501
AI US 2001-935316 A1 20010822 (9)
DT Utility
FS APPLICATION
LREP Michael P. Straher, Esquire., WOODCOCK WASHBURN LLP, One Liberty Place - 46th Floor, Philadelphia, PA, 19103
CLMN Number of Claims: 24
ECL Exemplary Claim: 1
DRWN 3 Drawing Page(s)
LN.CNT 2307
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compositions and methods for enhanced intestinal drug absorption. The formulation comprises a first population of carrier particles comprising a drug and a bioadhesive compound and a second population of carrier particles comprising a penetration enhancer. The bioadhesive extends the residence time of the drug and its absorptive potential across the portion of the intestinal mucosa made permeable by the penetration enhancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 17 OF 29 USPATFULL
AN 2003:93133 USPATFULL
TI Derivatized oligonucleotides having improved uptake and other properties
IN Manoharan, Muthiah, Carlsbad, CA, UNITED STATES
Cook, Phillip Dan, Carlsbad, CA, UNITED STATES
Bennett, Clarence Frank, Carlsbad, CA, UNITED STATES
PA Isis Pharmaceuticals, Inc. (U.S. corporation)
PI US 2003064492 A1 20030403
AI US 2002-154993 A1 20020523 (10)
RLI Continuation of Ser. No. US 2000-633659, filed on 7 Aug 2000, GRANTED, Pat. No. US 6395492 Division of Ser. No. US 1994-211882, filed on 22 Apr 1994, GRANTED, Pat. No. US 6153737 A 371 of International Ser. No. WO

1992-US9196, filed on 23 Oct 1992, UNKNOWN A 371 of International Ser. No. US 1991-782374, filed on 24 Oct 1991, ABANDONED Continuation-in-part of Ser. No. WO 1991-US243, filed on 11 Jan 1991, UNKNOWN Continuation-in-part of Ser. No. US 1990-463358, filed on 11 Jan 1990, ABANDONED Continuation-in-part of Ser. No. US 1990-566977, filed on 13 Aug 1990, ABANDONED

DT Utility
FS APPLICATION
LREP WOODCOCK WASHBURN LLP, ONE LIBERTY PLACE, 46TH FLOOR, 1650 MARKET STREET, PHILADELPHIA, PA, 19103
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2139
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Linked nucleosides having at least one functionalized nucleoside that bears a substituent such as a steroid molecule, a reporter molecule, a non-aromatic lipophilic molecule, a reporter enzyme, a peptide, a protein, a water soluble vitamin, a lipid soluble vitamin, an RNA cleaving complex, a metal chelator, a porphyrin, an alkylator, a pyrene, a hybrid photonuclease/intercalator, or an aryl azide photo-crosslinking agent exhibit increased cellular uptake and other properties. The substituent can be attached at the 2'-position of the functionalized nucleoside via a linking group. If at least a portion of the remaining liked nucleosides are 2'-deoxy-2'-fluoro, 2'-O-methoxy, 2'-O-ethoxy, 2'-O-propoxy, 2'-O-aminoalkoxy or 2'-O-allyloxy nucleosides, the substituent can be attached via a linking group at any of the 3' or the 5' positions of the nucleoside or on the heterocyclic base of the nucleoside or on the inter-nucleotide linkage linking the nucleoside to an adjacent nucleoside.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 18 OF 29 USPATFULL
AN 2003:60289 USPATFULL
TI **Oligonucleotide-folate conjugates**
IN Cook, Phillip Dan, Lake San Marcos, CA, United States
Manoharan, Muthiah, Carlsbad, CA, United States
Bhat, Balkrishen, Carlsbad, CA, United States
PA Isis Pharmaceuticals, Inc., Carlsbad, CA, United States (U.S. corporation)
PI US 6528631 B1 20030304
AI US 1998-98166 19980616 (9)
RLI Continuation-in-part of Ser. No. US 1993-117363, filed on 3 Sep 1993
DT Utility
FS GRANTED
EXNAM Primary Examiner: Riley, Jezia
LREP Woodcock Washburn LLP
CLMN Number of Claims: 42
ECL Exemplary Claim: 1
DRWN 9 Drawing Figure(s); 9 Drawing Page(s)
LN.CNT 3029
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB **Oligonucleotide-folate conjugates** are described wherein folates are conjugated to one or more sites on an oligonucleotide including the 2'-, 3'-, 5'-, nucleobase and internucleotide linkage sites. The folate can be attached via the .alpha.- or .gamma.-carboxylate, optionally through a linking group. Methods for the regiospecific synthesis of the conjugates are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

09567863

L1 ANSWER 19 OF 29 USPATFULL
AN 2003:57931 USPATFULL
TI Compositions and methods for non-parenteral delivery of oligonucleotides
IN Teng, Ching-Leou, San Diego, CA, UNITED STATES
Cook, Phillip Dan, Fallbrook, CA, UNITED STATES
Tillman, Lloyd, Carlsbad, CA, UNITED STATES
Hardee, Gregory E., Rancho Sante Fe, CA, UNITED STATES
Ecker, David J., Encinitas, CA, UNITED STATES
Manoharan, Muthiah, Carlsbad, CA, UNITED STATES
PI US 2003040497 A1 20030227
AI US 2001-29598 A1 20011221 (10)
RLI Continuation of Ser. No. US 1999-315298, filed on 20 May 1999, PENDING
Continuation of Ser. No. US 1998-108673, filed on 1 Jul 1998, PENDING
Continuation-in-part of Ser. No. US 1997-886829, filed on 1 Jul 1997, ABANDONED
DT Utility
FS APPLICATION
LREP Michael P. Straher, Woodcock Washburn LLP, One Liberty Place-46th Floor, Philadelphia, PA, 19103
CLMN Number of Claims: 26
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3600
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to compositions and methods which enhance the local and systemic uptake and delivery of oligonucleotides and nucleic acids via non-parenteral routes of administration. Pharmaceutical compositions comprising oligonucleotides disclosed herein include, for systemic delivery, emulsion and microemulsion formulations for a variety of applications and oral dosage formulations. It has also surprisingly been discovered that oligonucleotides may be locally delivered to colonic sites by rectal enemas and suppositories in simple solutions, e.g., neat or in saline. Such pharmaceutical compositions of oligonucleotides may further include one or more penetration enhancers for the transport of oligonucleotides and other nucleic acids across mucosal membranes. The compositions and methods of the invention are utilized to effect the oral, buccal, rectal or vaginal administration of an antisense oligonucleotide to an animal in order to modulate the expression of a gene in the animal for investigative, therapeutic, palliative or prophylactic purposes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 20 OF 29 USPATFULL
AN 2002:314673 USPATFULL
TI Derivatized oligonucleotides having improved uptake and other properties
IN Manoharan, Muthiah, Carlsbad, CA, UNITED STATES
Cook, Phillip Dan, Carlsbad, CA, UNITED STATES
Bennett, Clarence Frank, Carlsbad, CA, UNITED STATES
PA ISIS Pharmaceutical, Inc. (U.S. corporation)
PI US 2002177150 A1 20021128
AI US 2002-73718 A1 20020211 (10)
RLI Division of Ser. No. US 2000-633659, filed on 7 Aug 2000, GRANTED, Pat. No. US 6395492 Division of Ser. No. US 1998-211882, filed on 15 Dec 1998, GRANTED, Pat. No. US 6373826 Continuation-in-part of Ser. No. WO 1992-US9196, filed on 23 Oct 1992, UNKNOWN
DT Utility
FS APPLICATION
LREP Woodcock Washburn LLP, 46th Floor, One Liberty Place, Philadelphia, PA, 19103
CLMN Number of Claims: 44
ECL Exemplary Claim: 1

09567863

DRWN No Drawings
LN.CNT 2268
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Linked nucleosides having at least one functionalized nucleoside that bears a substituent such as a steroid molecule, a reporter molecule, a non-aromatic lipophilic molecule, a reporter enzyme, a peptide, a protein, a water soluble vitamin, a lipid soluble vitamin, an RNA cleaving complex, a metal chelator, a porphyrin, an alkylator, a pyrene, a hybrid photonuclease/intercalator, or an aryl azide photo-crosslinking agent exhibit increased cellular uptake and other properties. The substituent can be attached at the 2'-position of the functionalized nucleoside via a linking group. If at least a portion of the remaining liked nucleosides are 2'-deoxy-2'-fluoro, 2'-O-methoxy, 2'-O-ethoxy, 2'-O-propoxy, 2'-O-aminoalkoxy or 2'-O-allyloxy nucleosides, the substituent can be attached via a linking group at any of the 3' or the 5' positions of the nucleoside or on the heterocyclic base of the nucleoside or on the inter-nucleotide linkage linking the nucleoside to an adjacent nucleoside.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 21 OF 29 USPATFULL
AN 2002:133851 USPATFULL
TI Therapeutic uses of LNA-modified oligonucleotides
IN Orum, Henrik, Vaerlose, DENMARK
Koch, Troels, Copenhagen, DENMARK
Skouv, Jan, Espergade, DENMARK
Jakobsen, Mogens Havsteen, Vanlose, DENMARK
PI US 2002068709 A1 20020606
AI US 2000-747913 A1 20001222 (9)
PRAI US 1999-171873P 19991223 (60)
DT Utility
FS APPLICATION
LREP Dike, Bronstein, Roberts & Cushman, Intellectual Property Practice Group, Edwards & Angell, LLP, 130 Water Street, Boston, MA, 02109
CLMN Number of Claims: 26
ECL Exemplary Claim: 1
DRWN 3 Drawing Page(s)
LN.CNT 1596
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to therapeutic applications of LNA-modified oligonucleotides. In particular, the invention provides methods for treatment of undesired cell growth as well as treatment of inflammatory related diseases and disorders. Preferably, administration of an LNA-modified oligonucleotide modulates expression of a targeted gene associated with the undesired cell growth or an inflammatory related disease or disorder.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 22 OF 29 USPATFULL
AN 2002:122441 USPATFULL
TI Derivatized oligonucleotides having improved uptake and other properties
IN Manoharan, Muthiah, Carlsbad, CA, United States
Cook, Phillip Dan, Carlsbad, CA, United States
Bennett, Clarence Frank, Carlsbad, CA, United States
PA ISIS Pharmaceuticals, Inc., Carlsbad, CA, United States (U.S. corporation)
PI US 6395492 B1 20020528
AI US 2000-633659 20000807 (9)
RLI Division of Ser. No. US 211882, now patented, Pat. No. US 6153737
Continuation-in-part of Ser. No. US 1991-782374, filed on 24 Oct 1991

09567863

Continuation-in-part of Ser. No. WO 1991-US243, filed on 11 Jan 1991 Continuation-in-part of Ser. No. US 1990-463358, filed on 11 Jan 1990, now abandoned Continuation-in-part of Ser. No. US 1990-566977, filed on 13 Aug 1990, now abandoned
DT Utility
FS GRANTED
EXNAM Primary Examiner: Riley, Jezia
LREP Woodcock Washburn LLP
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 2292
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Linked nucleosides having at least one functionalized nucleoside that bears a substituent such as a steroid molecule, a reporter molecule, a non-aromatic lipophilic molecule, a reporter enzyme, a peptide, a protein, a water soluble vitamin, a lipid soluble vitamin, an RNA cleaving complex, a metal chelator, a porphyrin, an alkylator, a pyrene, a hybrid photonuclease/intercalator, or an aryl azide photo-crosslinking agent exhibit increased cellular uptake and other properties. The substituent can be attached at the 2'-position of the functionalized nucleoside via a linking group. If at least a portion of the remaining liked nucleosides are 2'-deoxy-2'-fluoro, 2'-O-methoxy, 2'-O-ethoxy, 2'-O-propoxy, 2'-O-aminoalkoxy or 2'-O-allyloxy nucleosides, the substituent can be attached via a linking group at any of the 3' or the 5' positions of the nucleoside or on the heterocyclic base of the nucleoside or on the inter-nucleotide linkage linking the nucleoside to an adjacent nucleoside.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 23 OF 29 USPATFULL
AN 2002:112898 USPATFULL
TI Targeted oligonucleotide conjugates
IN Manoharan, Muthiah, Carlsbad, CA, UNITED STATES
PA ISIS Pharmaceuticals, Inc. (U.S. corporation)
PI US 2002058639 A1 20020516
US 6525031 B2 20030225
AI US 2001-934424 A1 20010821 (9)
RLI Division of Ser. No. US 1998-97753, filed on 16 Jun 1998, GRANTED, Pat. No. US 6300319
DT Utility
FS APPLICATION
LREP Woodcock Washburn Kurtz, Mackiewicz & Norris LLP, One Liberty Place - 46th Floor, Philadelphia, PA, 19103
CLMN Number of Claims: 40
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1415
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides improved ingress of therapeutic and other moieties into cellular targets. In accordance with preferred embodiments, complexes are provided which carry primary moieties, chiefly therapeutic moieties, to such target cells. Such complexes preferably feature cell surface receptor ligands to provide specificity. Such ligands are preferably bound to primary moieties through polyfunctional manifold compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 24 OF 29 USPATFULL
AN 2002:92639 USPATFULL

09567863

TI Nucleosidic and non-nucleosidic folate conjugates
IN Cook, Phillip Dan, Lake San Marcos, CA, UNITED STATES
Manoharan, Muthiah, Carlsbad, CA, UNITED STATES
Bhat, Balkrishen, Carlsbad, CA, UNITED STATES
Guzzev, Andrel P., Carlsbad, CA, UNITED STATES
PA ISIS Pharmaceuticals, Inc. (U.S. corporation)
PI US 2002049163 A1 20020425
AI US 2001-973981 A1 20011009 (9)
RLI Division of Ser. No. US 1999-275505, filed on 24 Mar 1999, UNKNOWN
DT Utility
FS APPLICATION
LREP Michael P. Straher, WOODCOCK WASHBURN KURTZ, MACKIEWICZ & NORRIS LLP, One Liberty Place - 46th Floor, Philadelphia, PA, 19103
CLMN Number of Claims: 100
ECL Exemplary Claim: 1
DRWN 24 Drawing Page(s)
LN.CNT 4587
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB **Oligonucleotide-folate conjugates** are described wherein folates are conjugated to one or more sites on an oligonucleotide including the 2'-, 3'-, 5'-, nucleobase and internucleotide linkage sites. The folate can be attached via the .alpha.- or .gamma.-carboxylate, optionally through a linking group. Methods for the regiospecific synthesis of the conjugates are diclosed. Also disclosed are nucleosidic and non-nucleosidic linkers conjugated to folic acid and related folates.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 25 OF 29 USPATFULL
AN 2002:1321 USPATFULL
TI Nucleosidic and non-nucleosidic folate conjugates
IN Guzaev, Andrei P., Carlsbad, CA, United States
Cook, Phillip Dan, Fallbrook, CA, United States
Manoharan, Muthiah, Carlsbad, CA, United States
Bhat, Balkrishen, Carlsbad, CA, United States
PA ISIS Pharmaceuticals, Inc.,, Carlsbad, CA, United States (U.S. corporation)
PI US 6335434 B1 20020101
AI US 1999-275505 19990324 (9)
RLI Continuation-in-part of Ser. No. US 1998-98166, filed on 16 Jun 1998
DT Utility
FS GRANTED
EXNAM Primary Examiner: Riley, Jezia
LREP Woodcock Washburn Kurtz Mackiewicz & Norris LLP
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN 24 Drawing Figure(s); 24 Drawing Page(s)
LN.CNT 4283
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB **Oligonucleotide-folate conjugates** are described wherein folates are conjugated to one or more sites on an oligonucleotide including the 2'-, 3'-, 5'-, nucleobase and internucleotide linkage sites. The folate can be attached via the .alpha.- or .gamma.-carboxylate, optionally through a linking group. Methods for the regiospecific synthesis of the conjugates are diclosed. Also disclosed are nucleosidic and non-nucleosidic linkers conjugated to folic acid and related folates.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 26 OF 29 USPATFULL

09567863

AN 2001:173573 USPATFULL
TI Targeted oligonucleotide conjugates
IN Manoharan, Muthiah, Carlsbad, CA, United States
PA Isis Pharmaceuticals, Inc., Carlsbad, CA, United States (U.S. corporation)
PI US 6300319 B1 20011009
AI US 1998-97753 19980616 (9)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Riley, Jezia
LREP Woodcock Washburn Kurtz Mackiewicz & Norris LLP
CLMN Number of Claims: 25
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1642
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides improved ingress of therapeutic and other moieties into cellular targets. In accordance with preferred embodiments, complexes are provided which carry primary moieties, chiefly therapeutic moieties, to such target cells. Such complexes preferably feature cell surface receptor ligands to provide specificity. Such ligands are preferably bound to primary moieties through polyfunctional manifold compounds.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 27 OF 29 USPATFULL
AN 2000:161133 USPATFULL
TI Derivatized oligonucleotides having improved uptake and other properties
IN Manoharan, Muthiah, Carlsbad, CA, United States
Cook, Phillip Dan, Carlsbad, CA, United States
Bennett, Clarence Frank, Carlsbad, CA, United States
PA ISIS Pharmaceuticals, Inc., Carlsbad, CA, United States (U.S. corporation)
PI US 6153737 20001128
AI US 1994-211882 19940422 (8)
WO 1992-US9196 19921023
19920422 PCT 371 date
19920422 PCT 102(e) date
RLI Continuation-in-part of Ser. No. US 1991-782374, filed on 24 Oct 1991, now abandoned which is a continuation-in-part of Ser. No. WO 1991-US243, filed on 11 Jan 1991 which is a continuation-in-part of Ser. No. US 1990-463358, filed on 11 Jan 1990, now abandoned And a continuation-in-part of Ser. No. US 1990-566977, filed on 13 Aug 1990, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Riley, Jezia
LREP Woodcock Washburn Kurtz Mackiewicz & Norris LLP
CLMN Number of Claims: 34
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2474
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Linked nucleosides having at least one functionalized nucleoside that bears a substituent such as a steroid molecule, a reporter molecule, a non-aromatic lipophilic molecule, a reporter enzyme, a peptide, a protein, a water soluble vitamin, a lipid soluble vitamin, an RNA cleaving complex, a metal chelator, a porphyrin, an alkylator, a pyrene, a hybrid photonuclease/intercalator, or an aryl azide photo-crosslinking agent exhibit increased cellular uptake and other properties. The substituent can be attached at the 2'-position of the functionalized

nucleoside via a linking group. If at least a portion of the remaining liked nucleosides are 2'-deoxy-2'-fluoro, 2'-O-methoxy, 2'-O-ethoxy, 2'-O-propoxy, 2'-O-aminoalkoxy or 2'-O-allyloxy nucleosides, the substituent can be attached via a linking group at any of the 3' or the 5' positions of the nucleoside or on the heterocyclic base of the nucleoside or on the inter-nucleotide linkage linking the nucleoside to an adjacent nucleoside.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 28 OF 29 USPATFULL
AN 1998:34055 USPATFULL
TI Antisense oligonucleotides targeting cooperating oncogenes
IN Calabretta, Bruno, Philadelphia, PA, United States
Skorski, Tomasz, Philadelphia, PA, United States
PA Thomas Jefferson University, Philadelphia, PA, United States (U.S. corporation)
PI US 5734039 19980331
AI US 1994-306691 19940915 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Guzo, David; Assistant Examiner: Schwartzman, Robert
LREP Seidel, Gonda, LaVorgna & Monaco, PC
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 16 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 2470
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Therapeutic combinations of two or more antisense oligonucleotides are provided. At least one first antisense oligonucleotide specific for a cytoplasmic oncogene or proto-oncogene and at least one second antisense oligonucleotide specific for a nuclear oncogene or proto-oncogene are combined for treatment of a neoplastic disease. The first antisense oligonucleotide may be specific for, e.g., a ras or raf gene, or an oncogene which codes for a protein tyrosine kinase. The nuclear gene-targeting antisense oligonucleotide preferably may be specific for a nuclear oncogene or proto-oncogene which encodes a transcriptional factor. The combined oligonucleotides have enhanced activity against neoplastic disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 29 OF 29 USPATFULL
AN 97:22656 USPATFULL
TI Selective inhibition of cell proliferation by vav antisense oligonucleotides
IN Gewirtz, Alan M., Philadelphia, PA, United States
PA The University of Pennsylvania, Philadelphia, PA, United States (U.S. corporation)
PI US 5612212 19970318
AI US 1993-152634 19931112 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Rories, Charles C. P.
LREP Seidel, Gonda, Lavorgna & Monaco, P.C.
CLMN Number of Claims: 18
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1204
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Antisense oligonucleotides specific for the vav proto-oncogene inhibit the proliferation of malignant, but not normal, myeloid cells. The

oligonucleotides are therefore useful in the treatment of leukemias, in particular, as bone marrow purging agents. The vav antisense oligonucleotides also selectively inhibit the formation of erythroid cell colonies without effect on megakaryocyte and granulocyte/macrophage colony formation. The oligonucleotides are therefore useful in treating disorders characterized by an elevated hematocrit due to overproduction of erythrocytes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=>